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Impact of seasonal cycles on host-pathogen dynamics and disease mitigation for *Batrachochytrium salamandrivorans*

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ABSTRACT

Seasonal cycles have a demonstrated effect on the dynamics of human and animal diseases. However, their quantitative implications for disease mitigation in wildlife are less well studied. We quantitatively investigate the effect of seasonality on chytridiomycosis caused by *Batrachochytrium salamandrivorans* in European fire salamanders *(Salamandra salamandra)*. Floquet theory is a mathematical tool that allows the analysis of periodic systems. In epidemiology, it can be used to study the fate of a un-/managed host population when confronted with a new pathogen. Based on this theory, we develop a novel metric that captures outbreak dynamics similarly to the non-seasonal basic reproduction number R_0, but also accounts for seasonal cycles. We use this Floquet-R_0 to determine the management needed to defend a susceptible host population from disease outbreaks. In the *B. salamandrivorans* case, we found a limited effect of seasonality on disease dynamics and mitigation for two hypothetical European fire salamander populations with different seasonal cycles. However, a general model analysis suggested that Floquet-R_0 could deviate up to ±33% from the non-seasonal R_0, thus leading to insufficient or unnecessary management if seasonality is ignored. We recommend considering seasonal cycles – especially activity cycles with two peaks – when planning mitigation for chytridiomycosis and other wildlife diseases, because they add a considerable layer of uncertainty to analysis and decision-making. The Floquet-R_0 metric we present is an intuitive tool to quantitatively evaluate seasonality of disease and its influence on management.

1. Introduction

The influence of seasonality on disease dynamics has been reported by disease ecologists over the last few decades, in theory (Keeling and Rohani, 2008) as well as in human and wildlife systems (Dowell, 2001). Seasonal disease dynamics may be the result of a variety of underlying seasonal processes, such as fluctuations in parasite transmission or in host aggregation patterns at the population and individual level (Altizer et al., 2006). For humans, prominent examples include the increased incidence of measles when children aggregate during school terms (Fine and Clarkson, 1982) and of malaria during seasonal rains that favor reproduction of the mosquito vector (Hoshen and Morse, 2004). In wildlife diseases, the influence of seasonal fluctuations has been demonstrated for several host taxa (Altizer et al., 2004; Begon et al., 2009). A particularly well-studied

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example is the fungal disease chytridiomycosis caused by *Batrachochytrium dendrobatidis*, whose incidence and impacts have been shown to fluctuate seasonally in a broad range of geographic and climatic settings, correlating in particular with environmental temperatures that determine fungal activity and growth (Conradie et al., 2011; Kriger and Hero, 2007; Petersen et al., 2016; Ruggeri et al., 2015).

When seasonal cycles influence the impacts of disease on wildlife host species, they become intuitively relevant for mitigation plans, adding to the already considerable challenges faced by managers (Joseph et al., 2013). In human systems, policy-making increasingly reflects the epidemiological consequences of seasonality (Grassly and Fraser, 2006). For example, annual vaccination campaigns against influenza are timed to maximize cover during the expected peak season in autumn-winter (Lee et al., 2009). For wildlife diseases such as amphibian chytridiomycosis, however, assessments of the implications of seasonality for conservation have been mostly limited to qualitative considerations about the timing of monitoring surveys (e.g. Kriger and Hero, 2007).

In this study, we seek to fill this gap for amphibian chytridiomycosis caused by a pathogen for which the possible effects of seasonality have not been investigated to date, the chytrid fungus *Batrachochytrium salamandrivorans* (*Bsal*; Martel et al., 2013). This fungus, believed to have recently entered Europe from its native range in Asia (Martel et al., 2014), has driven the collapse of populations of fire salamanders (*Salamandra salamandra*) in the Netherlands and Belgium (Spitzen-van der Sluijs et al., 2016) and threatens to cause massive biodiversity loss in Europe and North America (Martel et al., 2014). Earlier studies have analyzed the epidemiology of *Bsal* and derived management recommendations for a short time window reflecting the duration of a typical outbreak (e.g. three months: Canessa et al., 2018; Schmidt et al., 2017).

In this study, we investigate how *Bsal*-host dynamics and the management required to mitigate the disease change with seasonal cycles in susceptible fire salamander hosts (*Salamandra salamandra*). We analyze an epidemiological model using Floquet theory, a mathematical tool named after the mathematician Gaston Floquet (1847–1920) that allows the analysis of periodic differential equations (Klausmeier, 2008; Mitchell and Kribs, 2017; Tian and Wang, 2015). In epidemiology, Floquet theory can be used to study what happens to a population of susceptible hosts when some infected individuals enter: do perturbations eventually vanish (the disease dies out) or increase (the disease remains in the population)? And how do seasonal cycles change the management required to mitigate the impacts of disease?

2. Methods

2.1. Epidemiological model with seasonally varying coefficients

We study the effect of different seasonal cycles using a dynamical epidemiological model with two compartments, susceptible $S(t)$ and infected individual $I(t)$ (henceforth simply S and I), and time-varying coefficients (Eq. (1)).

$$\begin{aligned} \frac{dS}{dt} &= \nu(t) - dS - c(t)p(t)SI \\ \frac{dI}{dt} &= c(t)p(t)SI - (\delta(t) + d)I \end{aligned} \tag{1}$$

If seasonal effects are ignored, in the absence of infected individuals ($I = 0$) the population dynamics are determined by natural mortality (at a rate d) and a constant inflow of metamorphosed larvae (ν). With infected individuals, pathogen transmission takes place at a rate β that we split into a contact rate (c) and the fraction of contacts resulting in successful transmissions (p), so that $\beta = cp$. Once individuals have been infected, in addition to natural mortality they suffer from *Bsal*-induced mortality at a rate δ. Current knowledge suggests that for fire salamanders the only exit from the infected compartment is death, without chance of recovery if left untreated (Stegen et al., 2017). Finally, we assume as an approximation that natural mortality does not show an appreciable seasonal cycle.

We base all time-varying coefficients in Eq. (1) on the general function $\theta(t) = \theta_0(1 - \theta_1 \cos(2\pi(t - \phi_\theta)))$, where θ is a placeholder for a given parameter. This function produces recurrent seasonal cycles on a yearly basis (the unit of time t is decimal years), with phase-lag $0 \leq \phi_\theta < 1$; θ_0 is the average value of $\theta(t)$ and θ_1 its amplitude. To set the phase lags for the four time-varying coefficients in Eq. (1), we assume that the activity of the pathogen follows a seasonal cycle caused by temperature and humidity, and the minimum of such a cycle in northern European temperate climates is at the beginning of the year (winter). Thus, we set all time lags ϕ_θ in relation to this underlying cycle. Further information on properties of the above-mentioned function can be found in the online Appendix to the paper, and case study-specific details in Table 1 and the subsection 2.4 Parameterization of study species.

2.2. Stability of disease-free state

The non-seasonal version of our model in Eq. (1) has two equilibria, a disease-free state and an endemic state. We focus on the disease-free state, asking whether it can be "defended" against a pathogen introduction, as this is the prominent management question for *Bsal* in its current and potential invasive range. In other words, the aim of management is to ensure the disease-free state remains stable. In Eq. (1) this disease-free state is characterized by the absence of infected individuals and

Table 1
Parameter values used for two hypothetical populations of fire salamanders (*Salamandra salamandra*) susceptible to the chytrid fungus *Batrachochytrium salamandrivorans*. The two populations reflect activity cycles with a hibernation and aestivation phase, respectively, and they were parameterized using data regarding populations in northwestern Europe and coastal regions of the Iberian Peninsula, respectively. «Online Appendix» in the column Source means that the respective derivation details can be found in the online Appendix to the paper.

Functions and parameters	Parameter values		Source
	Hibernation	Aestivation	
Time-varying larval inflow: $\nu(t) = \begin{bmatrix} 0, & 0<t<t_1 \\ \nu & t_1 \le t \le t_2 \\ 0 & t_2 \le t \le 1 \end{bmatrix}$	$\nu = 416$ larvae ha^{-1} y^{-1} $t_1 = 0.570$ y $t_2 = 0.720$ y	$\nu = 184$ larvae ha^{-1} y^{-1} $t_1 = 0.667$ y $t_2 = 0.837$ y	ν: online Appendix. t_1, t_2: online Appendix, based on (Rivera et al., 1999; Thiesmeier, 2004).
Carrying capacity:k_0 (approximation) or$S(t)$ (numerical analysis)	$k_0 = 500$ adults ha^{-1}	$k_0 = 250$ adults ha^{-1}	k_0: (Canessa et al., 2018; Rebelo and Leclair, 2003; Rivera et al., 1999; Stegen et al., 2017). $S(t)$: online Appendix.
Time-varying proportion of successful transmissions (upon contact): $p(t) = p_0 =$ constant	$p_0 = 1$	$p_0 = 1$	online Appendix.
Time-varying contact rate: $c(t) = c_0(1 - c_1 \cos(2\pi t))(1 - c_2 \cos(2\pi(t - \ell_c)))$	$c_0 = 0.7295$ y^{-1} $c_1 = 0.99$ (0.85) $c_2 = 0.90$ (0.85) $\ell_c = 0.48$ y (0.48)	$c_0 = 0.3647$ y^{-1} $c_1 = 0.85$ (0.84) $c_2 = 0.99$ (0.84) $\ell_c = 0.45$ y (0.45)	Estimated graphically from (Rivera et al., 1999; Spitzen-van der Sluijs et al., 2018; Stegen et al., 2017; Thiesmeier, 2004) (online Appendix). Values in brackets are used to explore an elevated activity during winter and summer (Fig. A4).
Natural mortality rate:$d =$ constant	$1/d = 8$ y	$1/d = 8$ y	(Sparreboom, 2014; Thiesmeier, 2004)
Time-varying *Bsal*-induced mortality rate: $\delta(t) = \delta_0(1 - \delta_1 \cos(2\pi t))$	$\delta_0 = 40.950$ y^{-1} $\delta_1 = 0.7780$	$\delta_0 = 43.40$ y^{-1} $\delta_1 = 0.6774$	δ_0, δ_1: online Appendix, based on (Stegen et al., 2017).

by a periodically fluctuating density of susceptible individuals around carrying capacity. In the following analysis, we will use both the explicit time-varying solution $S(t)$ and the approximation $S(t) = k_0 =$ constant (eqs. A1-A2).

For the non-seasonal variant of Eq. (1), a highly informative metric is the basic reproduction number $R_0 = c_0 p_0 k_0 (d + \delta_0)^{-1}$ (e.g. Keeling and Rohani, 2008), defined as the expected number of secondary cases originating from a primary infective case in a susceptible population. If $R_0 < 1$, the disease-free state is stable. For the seasonal version of the model, a time-varying measure can in principle be defined by substituting the time-varying functions into the above equation, giving $R_0(t) = c(t)p(t)k(t)(d + \delta(t))^{-1}$. However, this measure is not adequate to determine the stability of the disease-free state, not least because in a seasonal context it matters when the pathogen enters the susceptible population (Diekmann et al., 2012).

Instead, we derive an alternative metric to determine whether the system will remain disease-free. As mentioned in section 1. Introduction, Floquet theory allows the analysis of linear systems with periodic coefficients. In our case, the linear system is the linearized growth equation of the infected compartment, evaluated at the disease-free state, building the derivation of R_0 (further details in the online Appendix). Using Floquet theory, we analytically derive a key metric, the so-called Floquet exponent, which determines whether perturbations will vanish or amplify in the long-term, leading respectively to a stable or unstable disease-free state. The condition for a stable disease-free state is that the Floquet exponent must be smaller than zero.

For our model, the Floquet exponent can be explicitly derived (Eq. A4a) and rearranged so that the resulting expression − we call it $Floquet - R_0$ − has to be smaller than one for the disease-free state to be locally and linearly stable, providing a threshold analogous to $R_0 = 1$ for the non-seasonal model variant. For our study species, Floquet-R_0 can be simplified as

$$Floquet - R_0 = R_0 \frac{2 + c_1 c_2 \cos(2\pi \ell_c)}{m} \tag{2}$$

where R_0 is a composite parameter that contains average and/or time-invariant parameter values, and $m = \min(c(t)c_0^{-1}) + \max(c(t)c_0^{-1})$ is a scaling factor for $c(t)$. The amplitudes of the susceptibles at carrying capacity and of the proportion of successful transmissions upon contact are absent from Eq. (2) by choice (see subsection 2.4 Parameterization of study species), whereas the amplitude δ_1 (*Bsal*-induced mortality) does not affect $Floquet - R_0$. Note that assuming a one-peaked contact rate ($c_1 = 0$) leads to $Floquet - R_0 = R_0$ (e.g. Mitchell and Kribs, 2017).

2.3. Seasonality and disease mitigation

For non-seasonal epidemiological models, R_0 can often be directly used to calculate the proportion ϱ of a population to be achieved by management, for example by removal or vaccination, so that an initial infection will die out; for fire salamanders, Canessa et al. (2018) found that reducing initial density, k_0, probably represents the most effective mitigation action. For the non-seasonal variant of Eq. (1), the target proportion is simply $\varrho = {R_0}^{-1}$ (Diekmann et al., 2012). In the presence of seasonal

cycles, the target proportion becomes $\varrho_F = (Floquet - R_0)^{-1}$. Note, however, that applying ϱ_F may not preclude a pathogen from temporarily successfully invading a susceptible population, for example at times during a year when $R_0(t)$ is increasing, approaching and exceeding $Floquet - R_0$.

2.4. Parameterization study species

Because $Floquet - R_0$ is largely affected by contact rate parameters (Eq. (2)), we explored the influence of seasonality on *Bsal*-host dynamics by comparing two populations of fire salamanders with different seasonal cycles of activity, corresponding to a different time-varying contact rate $c(t)$. Published literature shows most fire salamander populations exhibit two seasonal peaks of activity: a main peak in autumn (breeding) and a smaller one in spring (deposition of larvae, earlier in the southern population), while metamorphosed individuals emerge from the water in summer (Thiesmeier, 2004). We compared two alternative patterns. First, a population in which fire salamanders show a greatly reduced activity period in winter and maintain some level of activity during summer. This type of activity pattern, which we refer to as "hibernation", may be found for example in populations in north-western Europe (Thiesmeier, 2004), at the front of the *Bsal* invasion (Spitzen-van der Sluijs et al., 2016). Second, a population in which fire salamander activity continues during winter, but is greatly reduced during the warmer summer months (such as the pattern reported for some populations in NE Spain; Rivera et al., 1999). We refer to this second pattern as "aestivation". We used published information either directly to parameterize the seasonal functions $(\nu(t),\ \delta(t))$ or indirectly, manually setting parameter values so that functions would graphically reproduce available data $(c(t))$. For both populations, we parameterized $c(t)$ assuming it reflects data on activity above ground. To assess the effect of this assumption, we additionally explored parameter values leading to an activity level of approximately 25% in winter and summer, compared to the peak in autumn (Fig. A4): such an increased activity might stem, for example, from favorable belowground conditions in burrows. For both host populations, we set $p_1 = k_1 = 0$, leading to Eq. (2) as explained in the online Appendix to the paper: we disregarded seasonality in the proportion of successful transmission, $p(t)$, in the absence of evidence to the contrary, and we set the susceptibles' dynamics, $S(t)$, to a constant (k_0) as an approximation. To assess the effect of uncertainty on our results, we performed an elasticity analysis on Floquet-R_0. Further, to gauge the accuracy of Eq. (2) as an approximation, we additionally solved $Floquet - R_0$ numerically, using all available information such as time-varying larval inflow (Eq. (A1)). All parameter values can be found in Table 1, and further method details in the online Appendix to the paper.

First, we carried out a general analysis of our model, to identify parameter combinations that lead to the greatest deviations of Floquet-R_0 from the non-seasonal R_0. Second, we analyzed the model for the sets of parameters we collected for the two hypothetical populations, calculating Floquet-R_0 and the target proportions required to avoid *Bsal* outbreaks. Finally, we performed an elasticity analysis on Floquet-R_0.

3. Results

The general analysis of the model revealed that the more asymmetrical the activity peaks are during a year, the lower Floquet-R_0 will be, and consequently, the less effort needed for mitigation (Fig. A2 and A3). The maximum proportional differences between the non-seasonal R_0 and Floquet-R_0 (see Eq. (2)) are approximately ±33%. The maximum increase occurs with two different contact rate cycles ($c_1 = 0.5$ and $c_2 = 1$ and vice versa, both with $\ell_c = 0.5$), i.e. with a complete diapause in winter and slightly reduced activity in summer, and vice versa (Fig. 1a). The maximum decrease occurs with $c_1 = c_2 = 1$ and $\ell_c = 0.3\overline{3}$, i.e. a high peak of contact rates in autumn with a small peak in early spring with two complete diapauses in between (Fig. 1b).

In comparison, our estimates of the seasonal cycles in the two hypothetical fire salamander populations were less markedly asymmetrical (Fig. 1b). As a result, we calculated a Floquet-R_0 of 8.27 for a hibernating population (Fig. 2a) and 1.92 for an aestivating population (Fig. 2b), meaning that in these cases explicitly accounting for seasonal effects only reduces R_0 (8.88 and 2.13, respectively) by approximately 7% and 10% respectively. The Floquet-R_0 values calculated numerically (Eq. (A3)) closely matched the analytically derived ones, suggesting Eq. (2) provided a reliable approximation (hibernating: 8.33; aestivating: 1.92). Finally, assuming a rather high activity level of approximately 25% in summer and winter, compared to peak-activity in autumn (Fig. A4), marginally affected our results: for the two populations, we calculated Floquet-$R_0 = 8.22$ and Floquet-$R_0 = 1.80$, respectively.

When considering management requirements for the two study populations, we found only a limited difference between the target proportions based on R_0 and Floquet-R_0, respectively ϱ and ϱ_F, both for hibernating (approximately $\varrho_F = 12\%$ and $\varrho = 11\%$, Fig. 2c), and aestivating populations (approximately $\varrho_F = 52\%$ and $\varrho = 47\%$, Fig. 2d). Thus, for our estimates of these two specific cases, basing management planning on Floquet-R_0 would suggest only marginally lower effort. For comparison, the maximum potential deviations of Floquet-R_0 from its non-seasonal version imply that the target proportion ϱ_F will lie in the range $0.75\varrho \leq \varrho_F \leq 1.5\varrho$: this means that in case of a maximum deviation the target proportion will be either too high $(\varrho_F = 0.75\varrho)$ and thus insufficient to prevent an outbreak, or too low $(\varrho_F = 1.5\varrho)$ and thus leading to unnecessary removal of susceptibles (Fig. A6). Note that, as explained in the section 2. Methods, successful management based on Floquet-R_0 does not necessarily prevent a pathogen from temporarily invading a host population with success. Deterministically, if managers wish to avoid even a potential temporary outbreak of *Bsal*, the target proportions should be as small as approximately 5%

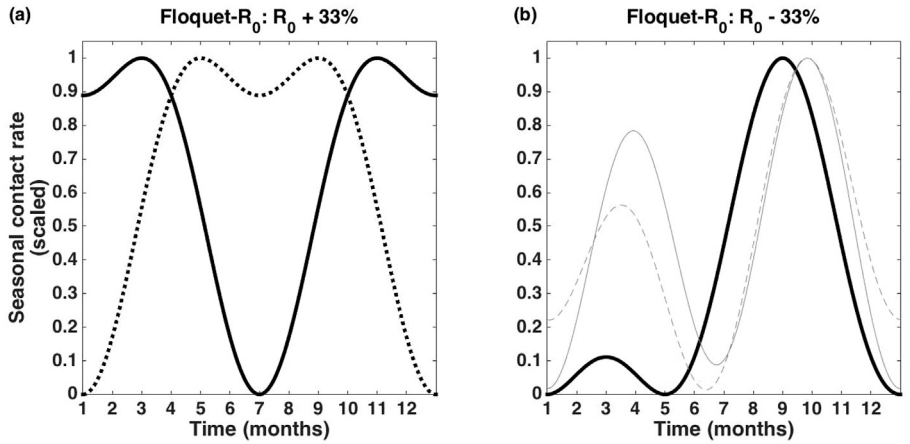

Fig. 1. Seasonal activity patterns leading to the highest deviations of Floquet-R_0 from R_0. **(a)** Seasonal contact rate cycles (scaled) resulting in the maximum proportional increase of Floquet-R_0 (+33%): $c_1 = 0.5$, $c_2 = 1.0$, $\wr_c = 0.50$ (solid line), and $c_1 = 1.0$, $c_2 = 0.5$, $\wr_c = 0.50$ (dotted line). **(b)** Seasonal contact rate cycle (scaled) resulting in the maximum proportional decrease of Floquet-R_0 (−33%): $c_1 = 1.0$, $c_2 = 1.0$, $\wr_c = 0.3\overline{3}$; in comparison (grey lines) the host-specific scaled contact rate cycles for our two hypothetical populations (solid: hibernation, dashed: aestivation; see also Fig. A1). The above-mentioned parameter values are derived from the general analysis in Fig. A2.

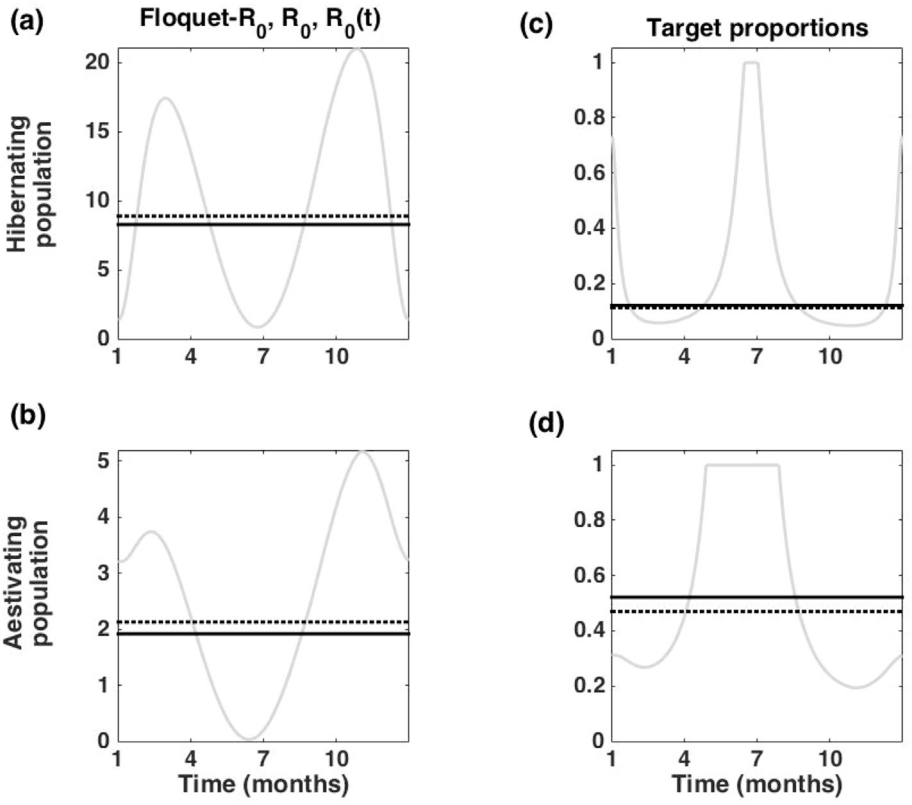

Fig. 2. Floquet-R_0, R_0, $R_0(t)$ (panels a–b) and the respective target proportions to be achieved by management (panels c–d) for two fire salamander populations with different seasonal activity patterns (row labels). Solid black lines are based on Floquet-R_0, and dotted black lines are based on non-seasonal R_0; in comparison, grey lines are based on $R_0(t)$.

(hibernating) or 20% (aestivating) (Fig. 2c–d). Finally, the elasticity analysis suggested that uncertainty around the phase lag estimate ℓ_c exerts the strongest influence on Floquet-R_0 and ϱ_F (Fig. A5).

4. Discussion

Our results showed that a seasonal contact rate characterized by two peaks, and potentially by a phase lag, can strongly influence the dynamics of a *Bsal* outbreak in a susceptible population. Our seasonal metric Floquet-R_0 can be smaller or greater than the non-seasonal basic reproduction number R_0 by as much as ±33%. When Floquet-R_0 is higher than R_0, basing mitigation on the non-seasonal metric risks falling short of the objectives, because management is insufficient to prevent an outbreak that could break the long-term stability of the disease-free state. Conversely, if Floquet-R_0 is lower than R_0, mitigation based on the latter may be unnecessarily heavy, aiming towards a target proportion that is higher than needed (which, depending on the treatment, could mean that too many animals are removed, or that the management effort is unnecessarily high).

Using the parameter estimates we derived from the literature, the seasonal cycles in our two hypothetical fire salamander populations did not lead to major differences between Floquet-R_0 and the non-seasonal R_0 (henceforth simply R_0). In those two cases, using Floquet-R_0 to inform management would not lead to major shifts in the recommended mitigation strategy. However, the maximum potential deviations of Floquet-R_0 from R_0 we identified (±33%) indicate that seasonality affecting *Bsal*-induced chytridiomycosis can have important implications for the conservation of susceptible hosts, particularly because the current uncertainty around the *Bsal*-host system means those are not simply theoretical extremes, but could actually occur in nature. Although little is known about *Bsal*-host seasonal cycles, several studies have highlighted seasonal fluctuations in the prevalence and intensity of *B. dendrobatidis* (*Bd*) infections, mostly linked to temperature and rainfall conditions (Conradie et al., 2011; Kriger and Hero, 2007). Lenker et al. (2014) reported peak prevalence and infection loads in spring and autumn in amphibians in New York State in the USA, with lowest points during high temperature periods in summer. Ruggeri et al. (2015) observed a similar pattern in Brazil, suggesting cooler temperatures could drive optimal pathogen growth but also host immunosuppression. However, Weinstein (2009) observed *Bd* infection in *Batrachoseps* salamanders in spring but not in autumn, although climate conditions were similar, and hypothesized that salamanders might either die or recover from the disease during the warmer months, indicating an interaction between pathogen and host seasonality; salamander density and inter-annual rainfall variation were also suggested as drivers of *Bd* cycles. Spitzen-van der Sluijs et al. (2017) also found seasonal and inter-annual fluctuations of *Bd* infection in *Bombina variegata* in the Netherlands, suggesting a combination of both host activity patterns and optimal temperature conditions for the fungus.

Behavioral adaptations of host species might also weaken the link between environmental temperatures and *Bsal* growth in the wild (for example if infected individuals expose themselves to higher temperatures). In our study, summer temperatures in the Iberian peninsula can increase beyond the survival limits for *Bsal*, but fire salamanders hosts are unlikely to ever experience those air temperatures, instead retreating into burrows and crevices that present more stable conditions. These refugia may be optimal locations for *Bsal* growth and transmission, or simply places in which infected animals become lethargic and die in isolation, interrupting disease spread. Caudate hosts aestivating in crayfish burrows or forming desiccation-resistant cocoons have been suggested as potential reservoirs of *Bd* in subtropical climates where summer temperatures would otherwise be unviable for the fungus (Chatfield et al., 2012). In our study, we assumed that contact rates among fire salamanders coincide with their observed activity cycles, an assumption that might be violated if, for example, spring activity by females involves fewer contacts than the autumn breeding season, leading to cycles more asymmetric than we suggested. Further research on such host-pathogen interactions is urgently needed.

Bsal can grow on multiple host species, which will further complicate disease dynamics at the community level; typically, the most abundant host species in the community will drive disease patterns at the community level (Altizer et al., 2006), so looking at a single host may provide too narrow an indication for management (Canessa et al, 2019). Finally, the environmental reservoir of free-living *Bsal* spores in the environment, replenished by spore-shedding infected hosts, is also likely to be affected by seasonal fluctuations in temperature and humidity (Stegen et al., 2017). The effect of multiple hosts and environmental reservoir on *Bsal* dynamics is still being clarified (Canessa et al., 2019), and currently there is no available information about their seasonal cycles. In the online Appendix, we illustrate how such information can be incorporated in our model when it becomes available. Our recommendation under the current knowledge is to act conservatively, targeting the environmental reservoir as drastically as possible, for example by environmental disinfection with antifungals (Bosch et al., 2015).

Even within the *Bsal*-caudate host system, broad inter- and intra-specific differences in seasonal cycles can complicate the generalization of the results. For example, although the general hibernation/aestivation pattern we have described covers most populations of *S. salamandra* in Europe, within the Iberian Peninsula alone, the activity peak due to females depositing larvae in water bodies can occur in October–April (Rivera et al., 1999), March–June (Martínez-Solano et al. 2006) or April–August (Montori, 1988). Such differences in turn may or may not lead to different combinations of host and pathogen cycles, depending for example on whether they simply reflect the same climatic pattern (i.e. salamanders are most active during the same temperature and humidity conditions, and these simply occur later or earlier in the year at different elevations or latitudes) or more complex dynamics (i.e. variable hydroperiods that might change the relationship between the cycles of host and pathogen). Such finer-scale variations remain to be evaluated and should be considered in management decisions that remain inevitably context-dependent.

Therefore, the potential for a strong influence of seasonality adds a layer to the uncertainty that already surrounds non-seasonal epizootic dynamics (Fig. A6). For reference, a previous study (Canessa et al., 2018) found the uncertainty around the non-seasonal R_0 for fire salamanders to range approximately from −40% to +50% of the mean, compared to the theoretical ±33% we identified between Floquet-R_0 and R_0. This additional uncertainty may further complicate mitigation decision-making. Of course, the final choice of mitigation strategy will depend on the management objectives. For example, a conservative strategy could simply assume the highest value of $R_0(t)$ in the seasonal cycle as the reference for management, provided the respective target proportion is feasible in terms of management effort, to ensure disease-free stability regardless of seasonality and avoiding even short-term outbreaks.

Moreover, in the case of *Bsal*, as for many wildlife diseases, mitigation options are severely limited, usually not going beyond the conceptual phase (Canessa et al., 2018), being extremely challenging to apply to wild populations (Blooi et al., 2015), or leading to only transient benefits (Geiger et al., 2017). Even where strategies are available, the extent to which they may be adjusted to seasonality varies. In the case of human influenza, vaccination strategies must strike a compromise between maximizing population coverage, maximizing the chance of addressing the most important viral strains for the coming season, and meeting production and logistic constraints (Sander et al., 2009). In the case of caudate *Bsal* hosts, some species may for example be too cryptic to be harvested in large proportions during their terrestrial phase, rendering removal actions unfeasible.

Given such a wide range of factors can affect the seasonality of disease, its effects, and its mitigation, managers and researchers may be tempted to ignore it altogether. In highly susceptible *Bsal* hosts such as fire salamanders, outbreaks in optimal conditions may be so violent that a non-seasonal model may still be entirely adequate to support decision-making (Canessa et al., 2018; Schmidt et al., 2017). However, because seasonality may have a large effect on long-term disease dynamics and consequently on mitigation choices, we recommend managers and their scientific advisors should at least be aware of it in their planning. Our proposed Floquet-R_0 provides a simple metric that is intuitively similar to the commonly used basic reproduction number R_0, and the corresponding outbreak threshold ($R_0 = 1$) used to guide management (Diekmann et al., 1990). In most cases, exact parameterization is likely to be difficult, particularly for emerging diseases such as *Bsal*. Nonetheless, formally elicited expert opinion may still be used to gain a general appreciation of the potential influence of seasonality on management options, ideally in combination with tools to address uncertainty, such as sensitivity and elasticity analyses. Decision-support methods (McCarthy, 2014) can then be used to judge the best option to choose in the face of risk deriving from seasonality, and the uncertainty that surrounds it.

Author contributions

CB set up and analyzed all mathematical models; SC provided all *Bsal*-related information and data; both authors wrote the manuscript.

Data accessibility

All relevant data are included in the text.

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Appendix A. Supplementary data

Supplementary data to this article can be found online at https://doi.org/10.1016/j.gecco.2019.e00551.

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